

753-65_PCT-US_revised_sequenc_ listing_ST25.txt
SEQUENCE LISTING

<110> POLYPHOR LTD.
Universitaet Zuerich

<120> Template fixed beta-hairpin mimetics and their use in phage display

<130> 753-65 PCT-US

<140> US 10/579104
<141> 2006-05-12

<150> PCT/EP 03/12783
<151> 2003-11-15

<160> 44

<170> PatentIn version 3.5

<210> 1
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<220>
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<400> 1

Val Arg Lys Lys
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<210> 2
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<212> PRT
<213> Artificial Sequence

<220>
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<210> 3
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<400> 3

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Trp Leu Asp Val

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<220>
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Obeidis, F.; Ostrem, J. A.; Drug Discovery Today, 1998, 3,
223-231.

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5

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1463.

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Tyr Ile Gly Ser Arg

1

5

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<220>
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Ile Lys Val Ala Val

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5

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<223> Key sequence known to occur in important physiologically active
peptides, see J. Biol. Chem., 1998, 273, 11001-11006 and
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<220>

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<221> misc_feature
 <222> (4)..(5)
 <223> Xaa can be any naturally occurring amino acid
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Pro Pro Arg Xaa Xaa Trp
 1 5

<210> 8
 <211> 10
 <212> PRT
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<220>
 <223> Hairpin mimetic derived from the general formula Cys-Z-Cys wherein the alpha amino group of the first amino acid is acetylated and wherein Z consists of 8 amino acids.

<220>
 <221> DISULFID
 <222> (1)..(10)

<220>
 <221> MOD_RES
 <222> (1)..(1)
 <223> ACETYLATION

<400> 8

Cys Lys Trp Phe Leu Ala His Tyr Ala Cys
 1 5 10

<210> 9
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 8 amino acids, and wherein both R1 and R2 consist of 2 amino acids.

<220>
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 <223> ACETYLATION

<220>
 <221> DISULFID
 <222> (3)..(12)

<400> 9

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 1 5 10

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<210> 10
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 <212> PRT
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<220>
 <223> hairpin mimetic derived from the general formula Cys-Z-Cys wherein the alpha amino group of the first amino acid is acetylated and wherein Z consists of 10 amino acids.

<220>
 <221> DISULFID
 <222> (1)..(12)

<220>
 <221> MOD_RES
 <222> (1)..(1)
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<400> 10

Cys Thr Lys Trp Phe Ser Asn His Tyr Gln Thr Cys
 1 5 10

<210> 11
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 <212> PRT
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<220>
 <223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 2 amino acids.

<220>
 <221> MOD_RES
 <222> (1)..(1)
 <223> ACETYLATION

<220>
 <221> DISULFID
 <222> (3)..(14)

<400> 11

Glu Thr Cys Thr Lys Trp Phe Ser Asn His Tyr Gln Thr Cys Thr Lys
 1 5 10 15

<210> 12
 <211> 12
 <212> PRT
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<220>
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<220>
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<220>
 <221> MOD_RES
 <222> (1)..(1)
 <223> ACETYLATION

<400> 12

Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys
 1 5 10

<210> 13
 <211> 16
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 2 amino acids.

<220>
 <221> MOD_RES
 <222> (1)..(1)
 <223> ACETYLATION

<220>
 <221> DISULFID
 <222> (3)..(14)

<400> 13

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 1 5 10 15

<210> 14
 <211> 16
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 2 amino acids.

<220>
 <221> MOD_RES
 <222> (1)..(1)
 <223> ACETYLATION

<220>
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 <222> (3)..(14)

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<400> 14

Asn Gly Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Lys Val
1 5 10 15

<210> 15

<211> 16

<212> PRT

<213> Artificial Sequence

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<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 2 amino acids.

<220>

<221> MOD_RES

<222> (1)..(1)

<223> ACETYLTATION

<220>

<221> DISULFID

<222> (3)..(14)

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Gly Gly Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Gly Gly
1 5 10 15

<210> 16

<211> 16

<212> PRT

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<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 2 amino acids.

<220>

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<223> ACETYLTATION

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<221> DISULFID

<222> (3)..(14)

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Glu Thr Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Thr Lys
1 5 10 15

<210> 17

<211> 18

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<212> PRT
<213> Artificial Sequence

<220>
<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 3 amino acids.

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> DISULFID
<222> (4)..(15)

<400> 17

Glu Leu Lys Cys Thr Lys Trp Phe Ser Asn His Tyr Gln Thr Cys Glu
1 5 10 15

Val Lys

<210> 18
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 3 amino acids.

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> DISULFID
<222> (4)..(15)

<400> 18

Lys Val Gly Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Gly
1 5 10 15

Leu Glu

<210> 19
<211> 18
<212> PRT

<213> Artificial Sequence

<220>

<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 3 amino acids.

<220>

<221> MOD_RES

<222> (1)..(1)

<223> ACETYLATION

<220>

<221> DISULFID

<222> (4)..(15)

<400> 19

Gly Gly Gly Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Gly
1 5 10 15

Gly Gly

<210> 20

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Hairpin mimetic derived from the general formula Cys-Z-Cys wherein the alpha amino group of the first amino acid is acetylated and wherein Z consists of 12 amino acids.

<220>

<221> DISULFID

<222> (1)..(14)

<220>

<221> MOD_RES

<222> (1)..(1)

<223> ACETYLATION

<400> 20

Cys Gly Thr Lys Trp Phe Ser Asn His Tyr Gln Thr Gly Cys
1 5 10

<210> 21

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 12 amino acids, and wherein

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both R1 and R2 consist of 2 amino acids.

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> DISULFID
<222> (3)..(16)

<400> 21

Glu Thr Cys Gly Thr Lys Trp Phe Ser Asn His Tyr Gln Thr Gly Cys
1 5 10 15

Thr Lys

<210> 22
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Core peptide sequence Z taken from the CDR L3 loop of an antibody described in Jiang, L. et al., Chimia, 2000,54, 558-563.

<400> 22

Leu Trp Tyr Ser Asn His Trp Val
1 5

<210> 23
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified core peptide sequence Z derived from core peptide sequence with the SEQ ID NO:22 containing a stabilizing beta-turn and a beta-sheet sequence according to Chou, P. Y., Fasman, G. D., J. Mol. Biol, 1977, 115, 135-175.

<400> 23

Lys Trp Phe Ser Asn His Tyr Gln
1 5

<210> 24
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Core peptide sequence Z constructed from peptide with the SEQ ID NO:25.

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<400> 24

Phe Leu Ala His Tyr Ala
1 5

<210> 25

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> oligopeptide which does not contain a dedicated stabilizing beta-turn sequence or a beta-sheet sequence according to Chou, P. Y., Fasman, G. D., J. Mol. Biol, 1977, 115, 135-175.

<400> 25

Leu Trp Tyr Ser Asn His Trp Val Lys Trp
1 5 10

<210> 26

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> oligonucleotide No. 1 used to construct insert DNA coding for template fixed hairpin mimetic of SEQ ID NO:10 and used to construct insert DNA coding for randomized library template fixed beta-hairpin mimetics having sequences according to SEQ ID NO:42.

<400> 26

catgcccggg tacctttcta ttctactct gaaacctgc

39

<210> 27

<211> 84

<212> DNA

<213> Artificial Sequence

<220>

<223> oligonucleotide No. 2 used to construct insert DNA coding for template fixed hairpin mimetic of SEQ ID NO:10.

<400> 27

catgtttcgg ccgagccacc acctttggtg caggtctgat aatggttgct gaaccatttg

60

gtgcaggttt cagagtgaga atag

84

<210> 28

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> DNA sequence coding for the peptide shown in SEQ ID NO:8.

<400> 28

tgcaaattgg ttctggcgca ttatgcgtgc

30

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<210> 29
 <211> 42
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:9.

 <400> 29
 gaaacctgca aatggttcct ggcgcattat gcgtgcacca aa 42

 <210> 30
 <211> 36
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:10.

 <400> 30
 tgcaccaa at ggttcagcaa ccattatcag acctgc 36

 <210> 31
 <211> 48
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:11.

 <400> 31
 gaaacctgca ccaa atggtt cagcaaccat tatcagacct gcaccaa 48

 <210> 32
 <211> 36
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:12.

 <400> 32
 tgcaccaa at gggttcctggc gcattatgcg acctgc 36

 <210> 33
 <211> 48
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:13.

 <400> 33
 ctggaatgca ccaa atggtt cctggcgc at tatgcgacct gcaaagtt 48

 <210> 34
 <211> 48

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<212> DNA
 <213> Artificial Sequence

<220>
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<400> 34
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<210> 35
 <211> 48
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:15.

<400> 35
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<210> 36
 <211> 48
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:16.

<400> 36
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<210> 37
 <211> 54
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:17.

<400> 37
 gaactgaaat gcaccaaattg gttcagcaac cattatcaga cctgcgaagt taaa 54

<210> 38
 <211> 54
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:18.

<400> 38
 aaagtgtggt gcaccaaattg gttcctggcg cattatgcga cctgcggtct ggaa 54

<210> 39
 <211> 54
 <212> DNA
 <213> Artificial Sequence

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<220>
<223> DNA sequence coding for the peptide shown in SEQ ID NO:19.

<400> 39
ggtaggtggct gcaccaaag gttcctggcg cattatgcga cctgcggcgg tggt          54

<210> 40
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA sequence coding for the peptide shown in SEQ ID NO:20.

<400> 40
tgcggtacca aatgggtcag caaccattat cagaccggtt gc          42

<210> 41
<211> 54
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA sequence coding for the peptide shown in SEQ ID NO:21.

<400> 41
gaaacctgcg gtaccaaag gttcagcaac cattatcaga ccggttgac caaa          54

<210> 42
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA sequence of randomized template fixed beta-hairpin mimetic
      Phage library.

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<221> misc_feature
<222> (10)..(11)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (13)..(14)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (16)..(17)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (28)..(29)
<223> n is a, c, g, or t

<220>
<221> misc_feature

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<222> (31)..(32)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (34)..(35)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (37)..(38)
<223> n is a, c, g, or t

<400> 42
gaaacctgcn nknknknkcg tggtagcnk nnknknknkt gcaccaaa

48

<210> 43
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Translated protein sequence of a randomized template fixed
beta-hairpin mimetic phage library

<220>
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<222> (3)..(14)

<220>
<221> MISC_FEATURE
<222> (4)..(6)
<223> Xaa can be any naturally occurring amino acid

<220>
<221> MISC_FEATURE
<222> (10)..(13)
<223> Xaa can be any naturally occurring amino acid

<400> 43

Glu Thr Cys Xaa Xaa Xaa Arg Gly Asp Xaa Xaa Xaa Xaa Cys Thr Lys
1 5 10 15

<210> 44
<211> 84
<212> DNA
<213> Artificial Sequence

<220>
<223> oligonucleotide No. 3 used to construct insert DNA coding for
randomized library template fixed beta-hairpin mimetics having
sequences according to SEQ ID NO:42.

<220>
<221> misc_feature
<222> (34)..(35)
<223> n is a, c, g, or t

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<220>
 <221> misc_feature
 <222> (37)..(38)
 <223> n is a, c, g, or t

<220>
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 <223> n is a, c, g, or t

<220>
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 <223> n is a, c, g, or t

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 <223> n is a, c, g, or t

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 <222> (58)..(59)
 <223> n is a, c, g, or t

<220>
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 <223> n is a, c, g, or t

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 nngcaggttt cagagtgaga atag 84